Empaveli™ (pegcetacoplan) – New orphan drug approval

- On May 14, 2021, the FDA announced the approval of Apellis' Empaveli (pegcetacoplan), for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH).

- PNH is caused by gene mutations that affect red blood cells. The condition is characterized by red blood cell destruction, anemia, blood clots, and impaired bone marrow function.

    - The disease affects 1 to 1.5 people per million. Individuals are typically diagnosed around ages 35 to 40.

- Empaveli is the first approved C3 inhibitor, a protein important in the compliment cascade.

- The efficacy of Empaveli was established in a randomized, open-label, active comparator-controlled, 16-week study in PNH patients who had been treated with a stable dose of Soliris® (eculizumab) for at least the previous 3 months and with hemoglobin (Hb) levels < 10.5 g/dL. Eligible patients entered a 4-week run-in period during which they received Empaveli in addition to their current dose of Soliris. Patients (N = 80) were then randomized to receive either Empaveli or their current dose of Soliris through the duration of the 16-week randomized controlled period (RCP). The primary endpoint was change from baseline to week 16 (during RCP) in Hb level.

    - At week 16, the adjusted mean change from baseline in Hb level was 2.37 g/dL in the group treated with Empaveli vs. -1.47 g/dL in the Soliris group, demonstrating an adjusted mean increase of 3.84 g/dL with Empaveli vs. Soliris ($p < 0.0001$).

- Empaveli carries a boxed warning for serious infections caused by encapsulated bacteria.

    - Because of the risk of serious infections, Empaveli is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

- Empaveli is contraindicated in:

    - Patients with hypersensitivity to pegcetacoplan or to any of the excipients
    - Patients who are not currently vaccinated against certain encapsulated bacteria, unless the risks of delaying Empaveli treatment outweigh the risks of developing a bacterial infection with an encapsulated organism
    - Patients with unresolved serious infection caused by encapsulated bacteria including *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae*.

- Additional warnings and precautions for Empaveli include infusion-related reactions, monitoring PNH manifestations after discontinuation of Empaveli, and interference with laboratory tests.

- The most common adverse reactions (≥ 10%) with Empaveli use were injection-site reactions, infections, diarrhea, abdominal pain, respiratory tract infection, viral infection, and fatigue.

- The recommended dose of Empaveli is 1,080 mg by subcutaneous (SC) infusion twice weekly via a commercially available infusion pump with a reservoir of at least 20 mL.

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  - Empaveli is intended for use under the guidance of a healthcare professional. After proper training in SC infusion, a patient may self-administer, or the patient's caregiver may administer Empaveli, if a healthcare provider determines that it is appropriate.
  - Refer to the Empaveli drug label for additional dosing and administration recommendations.

- In patients switching to Empaveli from Soliris, Empaveli should be initiated while continuing Soliris at its current dose. After 4 weeks, Soliris can be discontinued before continuing monotherapy with Empaveli. For patients switching from Ultomiris® (ravulizumab), Empaveli should be initiated no more than 4 weeks after the last dose of Ultomiris.

- Apellis' launch plans for Empaveli are pending. Empaveli will be available as a 1,080 mg/20 mL single-dose vial.